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EXAMINER	
GOLDBERG, JEANINE ANNE	

ART UNIT	PAPER NUMBER
1634	19

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/591,466	SCHAEWEN, ANTJE VON	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *April 15, 2002; June 24, 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,31-40,47 and 48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-3, 31-40, 47-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed April 15, 2002. Currently, claims 2-3, 31-40, 47-48 are pending. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.

2. Any objections and rejections not reiterated below are hereby withdrawn.

3. This action contains new grounds of rejection necessitated by amendment.

Priority

4. This application claims priority to PCT EP98/08001, filed December 1998 and foreign document 197 54 622.6, filed December 9, 1997.

Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d) prior to declaration of an interference, a translation of the foreign application should be submitted under 37 CFR 1.55 in reply to this action.

New Grounds of Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Newly amended Claims 2, 31-35, 37, 39, 47-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that

the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to any plant *N-acetylglucosaminyltransferase I*.

The specification teaches SEQ ID NO: 1, 3, 5 which are nucleic acid molecules asserted to be *N-acetylglucosaminyltransferase I* from tobacco, potato and Arabidopsis.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its ennoblement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...' required a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of specifies have been described by their complete

structure. In the instant case, Applicant has defined only three nucleic acid sequences within the scope of the claimed genus. It is unclear what the structure of plant *N-acetylglucosaminyltransferase I* are such that one of skill in the art may obtain a plant GnT I sequence or a potato GnT I sequence.

First, a determination of the level of predictability in the art must be made in that whether the level of skill in the art leads to a predictability of structure; and/or whether teachings in the application or prior art lead to a predictability of structure. The claims are directed methods which utilize N-acetyl glucosaminyl transferase I polynucleotides. With regard to the elected invention, the specification only describes a single protein and a single cDNA encoding that protein and fails to teach or describe any other polynucleotides that are related to SEQ ID NO: 1 within the limitations of the rejected claims. The specification provides no guidance as to how or where the disclosed polynucleotide can be modified yet still maintain the functionality required for the instant methods. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear,

concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention.

With respect to the Solanum tuberosum nucleic acids, applicant's have provided the description of a single species. Applicant's have not provided how to identify that a *N-acetylglucosaminyltransferase I* sequence is from potato origin as opposed to tobacco or Arabodopsis origin or additionally other origins. While applicant's may be entitled to homology language with functional language, Applicant's have not described Solanum tuberosum nucleic acids encoding *N-acetylglucosaminyltransferase I.*

With respect to the hybridize under stringent conditions in part c of Claim 35, the claim is sufficiently broad such that the claim does not have a structure function relationship such that any nucleic acid which would hybridize under stringent conditions would be encompassed. Stringent conditions are defined on page 10 of the specification. These nucleic acids have not been either described nor enabled. Amendment of Claim 35 to encompass the limitations of Claim 36 would overcome the rejection since the claim would have both a structure and function relationship.

With respect to newly added percent identity limitations in Claim 35, the specification has not described nucleic acids of 70% identity with SEQ ID NO: 1; DNA encoding an amino acid sequence which shares an amino acid sequence of at least 75% with SEQ ID NO: 2. The written description guidelines provide Example 14 to illustrate a claim which meets the written description guidelines which contains both percentage identity and function of the variant. While this example is drawn to a protein example, the nucleic acid analysis is similar. There is actual reduction to practice of a

single disclosed species. The instant claims encompass allelic variants, splice variants, homologues and nucleic acids from additional sources. The specification has not described which regions of the nucleic acid of SEQ ID NO: 1 or nucleic acids encoding SEQ ID NO: 2 are critical to the function such that the skilled artisan would recognize which nucleic acids which are 70% identical with SEQ ID NO: 1 would have the same function.

In the application at the time of filing, there is no record or description which would demonstrate conception or written description of any plant or potato N-acetyl glucosaminyl transferase polynucleotide.

Response to Arguments

The response traverses the rejection. The response asserts Claims 35, 37, 39, 47-48 are adequately described. This argument has been reviewed but is not convincing. As provided in the Written Description Examples, Example 9 is directed to hybridization language. The example is directed to an isolated nucleic acid which hybridizes under highly stringent conditions to the complement of SEQ ID NO: 1 and encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity. The analysis of the example states, much like the instant case, there is a single species disclosed (a molecule consisting of SEQ ID NO: 1) that is within the scope of the claimed genus. The analysis provides that "since highly stringent hybridization conditions in combination with the coding function of the DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention". The instant claim 35 does not contain any function of the DNA.

Therefore, lacking this functional language, the claims do not meet written description since there is no structure/function relationship provided as required by the guidelines.

Moreover, the instant claims have been amended to include percentage identity limitations. This limitations have been treated above, in the rejection above.

As provided in the written description guidelines, "if the application as filed does not disclose the complete structure of the claimed invention as a whole" additional determination as to whether the specification discloses other relevant identifying characteristics sufficient to describe the claimed invention in such full, clear, concise and exact terms is considered. The instant claims drawn to percent identity and hybridization language do not provide a "complete structure", therefore, weighing additional considerations is required. The guidelines provide that "factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function". Moreover, the guidelines provide that disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. In the instant application, since the claims are drawn in part to partial structures, namely percent identity and hybridization language, a combination of identifying characteristics are required that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the

claimed species is sufficient. Therefore, addition of functional language would help to overcome the rejection.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112-Scope of Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Newly amended Claims 2-3, 31-34, 37-40, 47-48 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing glycoproteins which contain Man5GlcNAc2 by transforming plants, plant cells or parts of plants with antisense SEQ ID NO: 1 which encodes an Solanum *N-acetylglucosaminyltransferase I* and isolating the desired glycoprotein from the cultivated material, plants comprising the antisense SEQ ID NO: 1 which encodes a Solanum *N-acetylglucosaminyltransferase I*, does not reasonably provide enablement for a method of producing glycoproteins with contain minimal Man4GlcNAc2 using the sense construct of SEQ ID NO: 1 to produce glycoproteins by eliminating or reducing the activity of N-acetyl glucosaminyl transferase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

It is noted that with regard to specific sequences, a restriction requirement was set forth, and applicant elected methods which utilize SEQ ID NO: 1. The generic claims have been examined fully, and the claims which specifically recite multiple inventions have been examined insofar as they apply to the elected invention.

The claims are broadly drawn to methods of producing glycoproteins displaying Man5GlcNAc2 by transforming plants, plant cells or parts of plants with sense or antisense of SEQ ID NO: 1 which encodes an Solanum *N-acetylglucosaminyltransferase I* and isolating the desired glycoprotein from the cultivated material, plants comprising the sense or antisense SEQ ID NO: 1 which encodes a Solanum *N-acetylglucosaminyltransferase I.*

The specification teaches the human *N-acetylglucosaminyltransferase I* is 35% identical to the novel potato gene. The specification teaches transforming the binary antisense potato (SEQ ID NO: 1) GnTI constructs into Agrobacterium and into the potato plants and tobacco plants. The specification provides that the antisense suppression of complex glycoproteins was successful in the potato plant #439 (page 35, example 4). The antisense construct did not suppress the N-acetyl glycosaminyl transferase I in three other plants, namely #79, 404, 512 (Figure 5).

The art teaches a method of producing glycoproteins by cultivating mutant plant cells with cDNA encoding human *N-acetylglucosaminyltransferase I* which restores the wild-type phenotype of the plant cells (Gomez, PNAS, 1994, abstract). Gomez teaches that the cgl mutant of Arabidopsis lacks GnT I was cultured with cDNA encoding the

human GnT I which restores the wild-type phenotype. The art teaches an assay for GnTI (page 1830, col. 2).

Thus, neither the specification nor the art teaches how to make and use the invention as broadly as claimed. As noted above, the specification has only described three *N-acetylglucosaminyltransferase I* genes. This does not enable the skilled artisan to make additional sequences (see Description rejection above).

Moreover, while the art teaches that the sense human *N-acetylglucosaminyltransferase I* restores the wild-type phenotype of the plants cells, the art is silent with respect to the use of the antisense construct. The instant specification illustrates that the antisense construct suppresses the expression of GnTI in a single plant. Restoring wild-type activity is useful for the processing of the glycoproteins; antisense contructs may be useful for eliminating or reducing the activity of N-acetyl glucosaminyl transferase which in turn facilitates the production of recombinant glycoproteins. The claims have been amended to be directed to producing glycoproteins with GluNAc2Man5 wherein transformation with antisense or sense contructs results in the elimination or reduction of the activity of N-acetyl glucosaminyl transferase do not appear to be enabled for use with sense constructs. From the data in the specification a single antisense constructs appears to block expression such that complex glycan are not synthesized yielding large quantities of the GlucNAc2Man5. The art teaches that the sense construct restores the activity of N-acetyl glucosaminyl transferase. Therefore, it is unpredictable how the sense construct would eliminate or reduce the N-acetyl glucosaminyl trasferase in transgenic plants. The skilled artisan

would be required to perform undue and unpredictable experimentation to determine whether the sense construct would reduce or eliminate activity under certain conditions.

Moreover, it is noted that the instant claims encompass methods which utilize nucleic acids that are related to SEQ ID NO: 1 based on hybridization and percentage identity. However, Applicant provides no guidance for the regions of the disclosed gene *N-acetylglucosaminyltransferase I* which are essential or sufficient to encode *N-acetylglucosaminyltransferase I*, or for the regions of SEQ ID NO: 1 which are essential or sufficient to encode a *N-acetylglucosaminyltransferase I*. The claims encompass allelic variants, splice variants, homologues and nucleic acids from additional sources. The instant specification does not enable the skilled artisan how to use these variants of the *N-acetylglucosaminyltransferase I* nucleic acids. It is unpredictable that each of these nucleic acids which either are 70% identical with SEQ ID NO: 1, which are 75% identical with SEQ ID NO: 2 or which hybridize under stringent conditions to SEQ ID NO: 1 or parts thereof would share the same function. The skilled artisan would only be able to use those nucleic acids which have the same function and activity as SEQ ID NO: 1 and those which encode SEQ ID NO: 2. Undue trial and error experimentation would be required to screen to determine which of the additional plant *N-acetylglucosaminyltransferase I* genes which would reduce or eliminate activity of N-acetyl glucosaminyl transferase which in turn produces glycoproteins. The specification has not demonstrated which regions of the nucleic acid of SEQ ID NO: 1 or nucleic acids encoding SEQ ID NO: 2 are critical to the function such that the skilled artisan would recognize which nucleic acids which are 70% identical with SEQ ID NO: 1, are

75% identical with SEQ ID NO: 2 and parts thereof which would have the same function.

Response to Arguments

The response traverses the rejection. The response asserts that "sense constructs are enabled as well." "It is known in the art that a sense construct can lead to a hybridization phenomenon which affects or prevents translation of the Gntl gene". This argument has been reviewed but is not convincing because the instant specification does not provide any indication that the sense construct of SEQ ID NO: 1 eliminates or reduces Gntl activity. In fact, the introduction of the sense construct into plants has been demonstrated in the art to restore activity. Therefore, predictability that the sense construct will eliminate or reduce Gntl activity is unpredictable and would require undue experimentation to evaluate under which conditions the Gntl activity would be eliminated or reduced. With respect to Page 21, last paragraph cited by the response in support of their arguments, the specification is relying upon "assumed hybridization phenomena in tobacco according to the work of Faske et al". Faske et al. Teaches a full-length cDNA encoding NADP-MDH from pea introduced in the sense and antisense orientation into tobacco. First, the nucleic acid of Faske are different and are involved in different pathways. Secondly, the results of Faske to not indicate predictably that sense nucleic acids eliminate or reduce activity. While some of Faske's tranformants reduced or eliminated activity, several also showed significant overexpression. Therefore, it is unpredictable whether the sense orientation of SEQ ID NO: 1 when transformed will reduce or eliminate Gntl activity.

Thus for the reasons above and those already of record, the rejection is maintained.

Allowable Subject Matter

7. Claims drawn to "an isolated DNA comprising SEQ ID NO: 1" or "an isolated DNA comprising a DNA sequence encoding the amino acid sequence of SEQ ID NO: 2", "an isolated DNA sequence comprising a nucleic acid with 70% identity with SEQ ID NO: 1 and encodes a polypeptide having N-acetyl glucosaminyl transferase I activity", "a nucleic acid which hybridizes under stringent conditions to SEQ ID NO: 1 which encodes a polypeptide having N-acetyl glucosaminyl transferase I activity".

The closest prior art teaches a human nucleic acid which encodes a polypeptide having N-acetyl glucosaminyl transferase I activity. This sequence does not fall within the scope of the claims because, the instant potato nucleic acid is 59% identical with the human N-acetyl glucosaminyl transferase I. Moroever, the mouse, rat and round worm are not encompassed by the claims (see Figure 3A).

Conclusion

8. Claims 2-3, 31-35, 37-40, 47-48 are rejected. Claim 36 if written in independent format would be allowable.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Enewold Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday, Wednesday and Friday 7:00 a.m. to 5:30 p.m. and Tuesday and Thursday from 7:00 a.m. to 1:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg

Jeanine Enewold Goldberg
August 16, 2002

W. Gary Jones
Supervisory Patent Examiner
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